ronment prior to the start of the experiment. Tactile allodynia was tested by touching the plantar surface of the animals hind paw with von Frey hairs in ascending order of force (0.7, 1.2, 1.5, 2, 3.6, 5.5, 8.5, 11.8, 15. 1, and 29 g) until a paw withdrawal response was elicited. Each von Frey hair was applied to the paw for 6 seconds, or until a response occurred. Once a withdrawal response was established, the paw was retested, starting with the next descending von Frey hair until no response occurred. The highest force of 29 g lifted the paw as well as eliciting a response, thus represented the cut-off point. Each animal had both hind paws tested in this manner. The lowest amount of force required to elicit a response was recorded as withdrawal threshold in grams. When compounds were administered before surgery, the same animals were used to study drug effects on tactile, allodynia, and thermal hyperalgasia, with each animal being tested for tactile allodynia 1 hour after thermal hyperalgesia. Separate groups of animals were used for examination of tactile allodynia and thermal hyperalgesia when S-(+)-3-isobutylgaba was administered after surgery.

Statistics

Data obtained for thermal hyperalgesia was subjected to a one-way (analysis of variance) ANOVA followed by a Dunnett's t-test. Tactile allodynia results obtained with the von Frey hairs were subjected to an individual Mann Whitney t-test.

RESULTS

An incision of the rat plantaris muscle led to an induction of thermal hyperalgesia and tactile allodynia. Both nociceptive responses peaked within 1 hour following surgery and were maintained for 3 days. During the experimental period, all animals remained in good health.

Effect of Gabapentin. S-(+)-3-Isobutylgaba and Morphine Administered Before Surgery on Thermal Hyperalgesia

The single-dose administration of gabapentin 1 hour before surgery dose-dependently (3–30 mg/kg, s.c.) blocked development of thermal hyperalgesia with a MED of 30 mg/kg (FIG. **1**b). The highest dose of 30 mg/kg gabapentin prevented the hyperalgesic response for 24 hours (FIG. **1**b). Similar administration of S-(+)-3-isobutylgaba also dose-dependently (3–30 mg/kg, s.c.) prevented development of thermal hyperalgesia with a MED of 3 mg/kg (FIG. **1**c). The 30 mg/kg dose of S-(+)-3-isobutylgaba was effective up to 3 days (FIG. **1**c). The administration of morphine 0.5 hour before surgery dose-dependently (1–6 mg/kg, s.c.) antagonized the development of thermal hyperalgesia with a MED of 1 mg/kg (FIG. **1**a). This effect was maintained for 24 hours (FIG. **1**a).

Effects of Gabapentin, S-(+)-3-Isobutylgaba and Morphine Administered Before Surgery on Tactile Allodynia

The effect of drugs on development of tactile allodynia was determined in the same animals used for thermal hyperalgesia above. One hour was allowed between thermal hyperalgesia and tactile allodynia tests. Gabapentin dose-dependently prevented development of tactile allodynia with a MED of 10 mg/kg. The 10 and 30 mg/kg doses of gabapentin were effective for 25 and 49 hours, respectively (FIG. **2**b). S-(+)-3-Isobutylgaba also dose-dependently (3–30 mg/kg) blocked development of the allodynia response with a MED of 10 mg/kg (FIG. **2**c). This blockade of the nociceptive response was maintained for 3 days by the 30 mg/kg dose of S-(+)-3-isobutylgaba (FIG. **2**c). In contrast, morphine (1–6 mg/kg) only prevented the development of tactile allodynia for 3 hour postsurgery at the highest dose of 6 mg/kg (FIG. **2**a).

Effect of S-(+)-3-Isobutylgaba Administered 1 Hour After Surgery on Tactile Allodynia and Thermal Hyperalgesia

The allodynia and hyperalgesia peaked within 1 hour in all animals and was maintained for the following 5 to 6 hours. The s.c. administration of 30 mg/kg S-(+)-3-isobutylgaba 1 hour after surgery blocked the maintenance of tactile allodynia and thermal hyperalgesia for 3 to 4 hours. After this time, both nociceptive responses returned to control levels indicating disappearance of antihyperalgesic and antiallodynic actions (FIG. **3**).

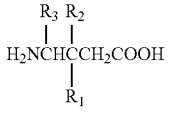
Gabapentin and S-(+)-3-isobutylgaba did not affect PWL in the thermal hyperalgesia test or tactile allodynia scores in the contralateral paw up to the highest dose tested in any of the experiments. In contrast, morphine (6 mg, s.c.) increased PWL of the contralateral paw in the thermal hyperalgesia test (data not shown).

The results presented here show that incision of the rat plantaris muscle induces thermal hyperalgesia and tactile allodynia lasting at least 3 days. The major findings of the present study are that gabapentin and S-(+)-3-isobutylgaba are equally effective at blocking both nociceptive responses. In contrast, morphine was found to be more effective against thermal hyperalgesia than tactile allodynia. Furthermore, S-(+)-3-isobutylgaba completely blocked induction and maintenance of allodynia and hyperalgesia.

What is claimed:

[1. A method for treating pain comprising administering a therapeutically effective amount of a compound of Formula I

I



or a pharmaceutically acceptable salt, diastereomer, or enantiomer thereof wherein

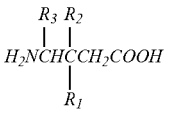
R_1 is a straight or branched alkyl of from 1 to 6 carbon atoms, phenyl, or cycloalkyl of from 3 to 6 carbon atoms;

R_2 is hydrogen or methyl; and

R_3 is hydrogen, methyl, or carboxyl to a mammal in need of said treatment.**]**

2. A method **[**according to claim **1]** *for treating pain comprising administering a therapeutically effective amount of a compound of Formula I*

I



or a pharmaceutically acceptable salt thereof, **[**wherein the compound administered is a compound of Formula I**]** wherein R_3 and R_2 are hydrogen, and R_1 is **[**—$(CH_2)_{0-2}$—i C_4H_9**]** *isobutyl* as an **[**(R),**]** (S)**[**, or (R,S)**]** isomer, *to a mammal in need of said treatment.*

[3. A method according to claim **1** wherein the compound administered is named (S)-3-(aminomethyl)-5-methylhexanoic acid and 3-aminomethyl-5-methylhexanoic acid.**]**

4. A method according to claim **[1]** *2* wherein the pain treated is inflammatory pain.

5. A method according to claim **[1]** *2* wherein the pain treated is neuropathic pain.